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Retrospective evaluation of 3% NaCl treatment in patients with symptomatic hyponatremia in the emergency department

Enver Özçete, Bahadır Arslan
Department of Emergency Medicine, Faculty of Medicine, Ege University, Izmir, Turkey

Abstract

Aim: As the most common electrolyte disorder in the Emergency Department, hyponatremia is a serious medical condition associated with a high risk of morbidity and mortality. Hypertonic saline is an effective treatment for symptomatic hyponatremia. This study aims to determine the effective variables in serum sodium elevation and overcorrection with 3% NaCl treatment in patients with symptomatic hyponatremia in the emergency department.

Material and Methods: In this study, we conducted a retrospective analysis of the efficacy of 3% NaCl treatment in symptomatic hyponatremic patients over 18 years of age. We described patients' characteristics and outcome variables.

Results: In our study, 582 patient files were reviewed. In total, 270 patients were excluded from the study. Ultimately, 312 patients were included in our study. The mean baseline sNa in the patients was 116±4.5 mmol/L. The most common Hypertonic 3% NaCl treatment was Rapid Intermittent Bolus with a rate of 64.4%. A minimum of 5 mmol/l increase in serum Na was observed in 36.5% of patients following the first treatment. In any period, 20.5% of patients had a rise in sNa of more than 10 mmol/L within the first 24 h.

Discussion: For treating symptomatic hyponatremia with 3% NaCl, a target serum Na of 125 mmol/L may be used along with a 5 mmol/L increase in serum Na. In the prevention of excessive serum Na elevation, 3% NaCl treatment in a volume smaller than baseline serum Na levels < 125 mmol/L may be considered.

Keywords

Hyponatremia, Hypertonic Saline, Emergency Department

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Corresponding Author: Enver Özçete, Department Of Emergency Medicine, Faculty of Medicine, Ege University, Izmir, Turkey.
E-mail: eozcete@gmail.com P: +90 505 594 39 36
Corresponding Author ORCID ID: https://orcid.org/0000-0002-1685-2369
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Introduction

Hyponatremia is the most common electrolyte disorder in the Emergency Department and is a serious medical condition associated with a high risk of morbidity and mortality [1]. The prevalence of hyponatremia in the emergency department is approximately 3-10% [2,3].

Hypertonic saline (3% NaCl) is an effective treatment for symptomatic hyponatremia [4-6]. While incomplete correction of hyponatremia may be insufficient to prevent life-threatening signs of cerebral edema, overcorrection resulting from prolonged use of hypertonic saline may result in osmotic demyelination syndrome (ODS) [7-10].

Hence, American and European guidelines recommend administering hypertonic saline in small, fixed boluses [11,12]. Hypertonic saline therapy can be administered as a rapid intermittent bolus (RIB) or as a slow continuous infusion (SCI) in patients with symptomatic hyponatremia. The Salsa Study, which compared these two applications, found that hypertonic saline for treating symptomatic hyponatremia was effective and safe without any difference in the risk of overcorrection, but recommended RIB treatment as the preferred treatment of symptomatic hyponatremia consistent with current guidelines [13].

In this study, we aimed to investigate the characteristics of symptomatic hyponatremic patients admitted to the emergency department treated with 3% NaCl and the efficacy of the treatments. We also aimed to determine the target serum sodium (sNa) elevation and the variables effective in overcorrection.

Material and Methods

This study has approval from University Ethics Committee (approval number: 23-1T/41). Patients over 18 years who presented to our emergency department between 01/01/2019 and 31/12/2021, who were found to have a sNa level of <125mmol/L in the baseline blood value taken in the ED and symptomatic hyponatremia based on the clinical manifestations and who were treated with 3% NaCl were included in the study. Moderate symptoms include nausea, headache, drowsiness, general weakness, and malaise. Meanwhile, severe symptoms include vomiting, stupor, seizure, and coma [11].

Anuric patients, on a routine dialysis program, had arterial hypotension (systolic blood pressure <90 mm Hg and mean arterial pressure <70 mm Hg), liver cirrhosis, blood glucose-corrected Na value of >125 mmol/L [14], chronic alcoholics, and patients with missing data were excluded.

The treatment of Symptomatic Hyponatremia is carried out in our emergency department using 150 ml of 3% NaCl administered by peripheral vascular access. As the RIB or SCI, patients were given 1-2 units of 3% NaCl for 20 minutes until symptom remission was achieved [11,12]. In some patients, 1 bolus treatment was administered over 20 min and then treatment was continued with SCI (0.5-1 ml/Kg/hour) depending on the control sNa level.

Data evaluation

Patients' complaints at admission, comorbidities, diuretic drugs used, demographic and clinical characteristics, patient diagnoses, laboratory test results, treatments administered, time of receiving control sNa, patient outcomes, and potential complications (Mortality, osmotic demyelination syndrome) were retrospectively recorded in the case report form. Patients were divided into groups according to the sNa value at the first presentation to the emergency department. Post-treatment sNa increases in the patients were calculated and groups were formed according to the amount of increase.

An elevation of 5 mmol/L sNa following the first treatment was accepted as a target correction in patients [11]. Moreover, patients with a sNa level of ≥125 mmol/L on their first and 24th Hour control were considered to have met the target. In any period, an increase of more than 10 mmol/L in sNa within the first 24 h was considered as overcorrection (overcorrection incidence is the number of individuals who developed overcorrection among the total number of participants) [11]. The length of stay of the patients in the emergency department was calculated. The rate of discharge from the emergency department or hospitalization of symptomatic HypoNa patients was evaluated.

Data were collected by one of the clinicians conducting the study. The other clinician conducted the statistical analysis.

Statistical analysis

Normally distributed continuous data were presented as mean and standard deviation, whereas non-normally distributed data were presented as median and interquartile range. Categorical variables were analyzed with frequency tables, and descriptive statistics were calculated for continuous variables. Independent sample t-tests and Mann–Whitney U tests were conducted to compare parametric and nonparametric continuous data, respectively. The Pearson Chi-square test was used to analyze categorical data in terms of groups. In all hypothesis tests, P <0.05 was considered significant. Odds ratios at 95% confidence interval (CI) of each parameter were calculated for each variable. Statistical analysis was conducted using IBM SPSS Version 25.0.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

A total of 582 patients were identified who were admitted to the emergency department between 01/01/2019 and 31/12/2021 and received 3% NaCl treatment. A total of 270 patients were excluded from our study, and 312 patients were included (Figure 1).

The mean age of the patients was 71.5±12.5 years and 64.1% were female. The mean baseline sNa was 116±4.5 mmol/L. With a rate of 64.4%, RIB was the most commonly administered Hypertonic 3% NaCl treatment. Hypertonic saline therapy was administered to patients in the emergency department and by the peripheral intravenous route. When the volume status of the patients was analyzed, hypovolemia was seen most frequently with a rate of 53.5%. The median value of the first control sNa time was 4 (4-6) h. Based on the sNa change in the 24th-hour control values, 76% of patients had a sNa increase of at least 5 mmol/L and 49.7% had a sNa level of >125 mmol/L. The target (5 mmol/L increase or sNa>125 mmol/L) was not achieved in 17% of patients. 3% NaCl treatment was discontinued in patients with a serum Na level of ≥125 mmol/L. The mean

Table 1. Demographic and laboratory characteristics of patients with symptomatic hyponatremia.

Variables	N:312	%
Female	112	35,9
Male	200	64,1
Mean age (years)	71,5±12,5	
Hypertension	203	65,1
Malignancy	97	31,1
Diabetes mellitus	90	28,8
Non-dialysis kidney failure	79	25,3
Congestive heart failure	26	8,3
Thiazide use	115	36,9
Furosemide use	52	16,7
Hypervolemic	71	22,8
Euovolemic	74	23,7
Hypovolemic	167	53,5
Mean Systolic BP (mmHg)	133,4±25,9	
Mean Diastolic BP (mmHg)	73,2±14	
Initial sNa mean mmol/l	116±4,5	
First Check sNa median time (Hours)	4 IQR (4-6)	
one receiving 3% NaCl treatment	128	41
Two receiving 3% NaCl treatment	117	37,5
sNa increase ≥5 mmol/L after initial treatment	114	36,5
sNa increase of ≥5 mmol/L or ≥125 mmol/L after initial treatment	137	43,9
Control sNa ≥125 mmol/L after initial treatment	64	20,5
sNa increase of <5 mmol/L or <125 mmol/L within the first 24 hours	53	17
Blood Glucose median-IQR (mg/dl)	125 (106-145)	
Creatinine median-IQR (mg/dl)	0,9, IQR (0,7-1,3)	
Potassium median-IQR (mmol/L)	4,3 IQR (3,7-4,7)	
Mean osmolarity (mOsm/kg)	250,4 (12,4)	
Median Time in the Emergency Department-IQR (minute)	1181,5 (685-1829)	

Data are expressed as numbers only, mean (standard deviation). sNa, Serum Sodium; BP, Blood pressure; RIB, Rapid intermittent bolus; SCI, Slow continuous infusion

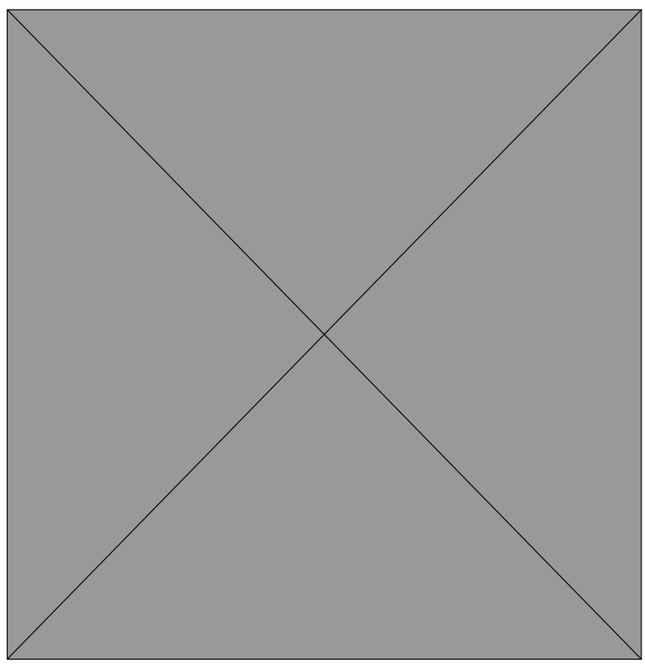

Figure 1. Study flow diagram.

Table 2. Variables affecting achieving target according to the first control sNa increase after hypertonic saline (3%NaCl) treatment in patients with symptomatic hyponatremia.

Variables	N(%) 312	Insufficient correction 175 (%56,1)	Sufficient correction 137 (%43,9)	P value	OR
RIB treatment	201 (64,4)	105 (%60)	96 (%70)	0,042	1,6 (0,9-2,5)
RIB + SCI treatment	91 (29,2)	57 (%32,5)	34 (%24,8)	0,085	0,7 (0,4-1,1)
SCI treatment	20 (6,4)	13 (%7,5)	7(%5,2)	0,278	0,7 (0,3-1,7)
One receiving 3% NaCl	128 (41)	59 (%33,7)	69(%50,4)	0,002	1,9 (1,3-3,2)
Two receiving 3% NaCl	117 (37,5)	66 (%37,7)	51(%37,2)	0,512	0,6 (0,6-1,6)
Female	200 (64,1)	112	88	0,531	0,9 (0,6-1,6)
Male	112 (35,9)	63	49		
Age ≥80 years	92 (29,5)	58 (33)	34 (25)	0,07	0,7 (0,4-1,1)
Hypovolemic	167 (53,5)	84 (48)	83 (61)	0,018	1,7 (1,1-2,6)
Hypervolemic	71 (22,8)	53 (30)	18 (13)	0	0,3 (0,2-0,6)
Initial sNa 120-125 mmol/l	57 (18,2)	20 (11)	37 (27)	0	2,9 (1,6-5,2)
Initial sNa115-120 mmol/l	147 (47,1)	97 (55)	50 (36)	0,001	0,5 (0,3-0,7)
Initial sNa 110-115 mmol/l	71 (22,8)	42 (24)	29 (21)	0,325	0,9 (0,5-1,5)
Initial sNa <110 mmol/l	37 (11,9)	16 (9)	21 (15)	0,067	1,8 (0,9-3,6)
Creatinine >1,3 (mg/dl)	81 (25,9)	41 (23)	40 (29)	0,153	1,3 (0,8-2,2)
Potassium <3,5 (mmol/L)	40 (12,8)	18 (10)	22 (16)	0,09	1,7 (0,9-3,3)
sNa increase <5 mmol/l in 24 h.	75 (24)	57 (33)	18 (13)	0	0,3 (0,2-0,6)
sNa increase 5-10 mmol/l in 24 h.	173 (55,5)	94 (54)	79 (58)	0,28	1,2 (0,7-1,8)
sNa increase ≥10 mmol/l in 24 h.	64 (20,5)	24 (14)	40 (29)	0,001	2,6 (1,5-4,6)
sNa ≥ 125mmol/l within the first 24 hours	155 (49,7)	67 (38)	88 (64)	0	2,9 (1,8-4,6)
inpatient	108 (34,6)	66 (38)	42 (31)	0,119	0,7 (0,5-1,2)
outpatient	204 (65,4)	109 (62)	95 (69)		

Data are expressed as numbers only, number (%), or mean (standard deviation). sNa, Serum Sodium; RIB, Rapid intermittent bolus; SCI, Slow continuous infusion; OR, Odds ratios.

osmolarity value was 250.4 (12.4) and 65.4% of the patients were discharged. The median length of stay in the emergency department was 1181.5 (685-1829) minutes. (Table 1)

As the most common presenting complaint, nausea and vomiting accounted for 27.2% of all visits. With a rate of 26.9%, thiazide-induced hyponatremia was the most common diagnosis.

In symptomatic hyponatremic patients, the variables affecting the target (5 mmol/L increase or sNa >125 mmol/L) initial Na change were admission sNa level, medications, patient's volume status, and RIB treatment. The fact that the patient was hypovolemic or RIB treatment was more effective than other treatments in changing the target sNa. The targeted sNa change was less achieved in hypervolemic patients.

Table 3. Characteristics of the overcorrection group after hypertonic saline (3% NaCl) treatment of symptomatic hyponatremia patients.

Variables	N 312	No overcorrection 248 (79,5)	Overcorrection 64 (20,5)	P-value	OR
RIB treatment	201 (64,4)	170 (69)	31 (48)	0,002	0,4 (0,2-0,8)
RIB + SCI treatment	91 (29,2)	62 (25)	29 (45)	0,002	2,5 (1,4-4,4)
SCI treatment	20 (6,4)	16 (6)	4 (6)	1	0,9 (0,3-2,9)
One receiving 3% NaCl	128 (41)	115 (46)	13 (20)	0	0,3 (0,2-0,6)
Two receiving 3% NaCl	117 (37,5)	90 (36)	27 (42)	0,234	1,3 (0,7-2,2)
Receiving at least three 3% NaCl	67 (21,5)	43 (17)	24 (38)	0,001	2,9 (1,6-5,2)
Female	200	158	42	0,448	0,9 (0,5-1,6)
Male	112	90	22		
Age ≥80 years	92 (29,5)	75 (30)	17 (27)	0,341	0,8 (0,5-1,5)
Hypovolemic	167 (53,5)	134 (54)	33 (52)	0,415	0,9 (0,5-1,6)
Hypervolemic	71 (22,8)	59 (24)	12 (19)	0,248	0,7 (0,4-1,5)
Initial sNa 120-125 mmol/l	57 (18,2)	56 (23)	1 (2)	0	0,05 (0,0-0,4)
Initial sNa115-120 mmol/l	147 (47,1)	127 (51)	20 (31)	0,003	0,4 (0,2-0,7)
Initial sNa 110-115 mmol/l	71 (22,8)	48 (19)	23 (36)	0,005	2,3 (1,3-4,3)
Initial sNa <110 mmol/l	37 (11,9)	17 (7)	20 (31)	0	6,2 (2,9-12,7)
Control sNa ≥125 mmol/L after initial treatment	64 (20,5)	55 (22)	9 (14)	0,101	0,6 (0,3-1,2)
sNa increase ≥5 mmol/L after initial treatment	114 (36,5)	75 (30)	39 (61)	0	3,6 (2-6,4)
sNa increase of ≥5 mmol/L or ≥125 mmol/L after initial treatment	137 (43,9)	97 (39)	40 (63)	0,001	2,6 (1,5-4,6)
Creatinine >1,3 (mg/dl)	81 (25,9)	55 (22)	26 (41)	0,003	2,4 (1,3-4,3)
Potassium <3,5 (mmol/L)	40 (12,8)	29 (12)	11 (17)	0,167	1,6 (0,7-3,3)
inpatient	108 (34,6)	91 (37)	17 (27)	0,084	0,6 (0,3-1,2)
outpatient	204 (65,4)	157 (63)	47 (73)		
control sNa ≥ 125mmol/l within the first 24 hours	155 (49,7)	113 (46)	42 (66)	0,003	2,3 (1,3-4,0)

Data are expressed as number only, number (%), or mean (standard deviation). sNa, Serum Sodium; RIB, Rapid intermittent bolus; SCI, Slow continuous infusion; OR, Odds ratios.

Overcorrection was observed more in the group with targeted change in the 24th hour. There was no difference between the mean admission sNa levels of the two groups (Table 2).

The effective factors for sNa overcorrection in patients were baseline sNa level at hospital admission, elevated creatinine levels, and the administration of RIB+SCI treatment. Overcorrection was less common among patients treated with furosemide in the emergency department (Table 3).

No mortality or osmotic demyelinating syndrome was detected in patients with severe hyponatremia who were followed -up and treated in the emergency department.

Discussion

For treating symptomatic hyponatremic patients with 3% NaCl in the Emergency Department, the factors affecting the target sNa increase of 5 mmol/L or sNa >125 mmol/L were found to be RIB treatment, patient volume status, and baseline sNa level. Overly rapid sNa correction was affected by receiving RIB+SCI treatment, elevated creatinine, baseline sNa level, and furosemide treatment in the emergency department.

The time to first control the sNa level was 4 IQR (4-6) hours. Since clinical findings related to hyponatremia are typically seen in sNa<125 mmol/L, one of our goals was to achieve a sNa level of ≥125 mmol/L. We achieved more of our targeted sNa change with RIB and one 3% NaCl. European Clinical Practice guidelines recommend a 5 mmol/L increase for treating symptomatic hyponatremia [11]. In 36.5% of our patients, we detected an increase of 5 mmol/L sNa at the first control. When the target sNa elevation was 5 mmol/L increase or the sNa level was ≥125 mmol/L, we reached our target in approximately 44% of patients. Hence, we are of the opinion that we administered less volume of 3% NaCl treatment to the patients. A sNa elevation of 5 mmol/L may not be necessary for every patient [15]. In 24% of our symptomatic patients with severe hyponatremia who were followed -up and treated in the emergency department, their symptoms regressed despite failure to increase the sNa level by 5 mmol/L within 24 hours.

For treating patients with symptomatic hyponatremia, 3% NaCl treatment is recommended either as RIB or as an SCI [11,12]. In our patient group, there were 29% of patients in whom 3% NaCl treatment was started as an SCI following RIB. In this patient group, overcorrection was 2.5 times more common than in the other treatment groups. It was found that SCI treatment was the least commonly applied treatment group (6%). In the Salsa study, RIB was recommended for treating severe hyponatremia. The most common treatment we employed was RIB (64%). When the three treatment groups were compared in the treatment of severe hyponatremia in the emergency department, RIB treatment was the one with less risk of overcorrection and more successful in reaching the target sNa level.

According to an American expert panel recommendation, overcorrection is defined as an increase in serum sodium of >10-12 mEq/L in any 24 h, or >8 mEg/L in patients at high risk of developing ODS [12]. Meanwhile, the European clinical practice guideline defines it as an increase in serum sodium levels >10 mEq/L in the first 24 h as overcorrection [11]. According to studies, there is still no consensus on the definition of overcorrection of hyponatremia among guidelines

[11,12, 16-20]. Furthermore, the incidence of overcorrection has been reported to be as high as 20% to 41% [16,17, 21-24]. In our study, overcorrection (sNa>10 mEq/L increase) was seen at a rate of 20.5%. Overcorrection occurred higher in baseline sNa level, high serum creatinine, and a minimum of three doses of 3% NaCl 150 mL. The mean baseline sNa at admission was lower in the overcorrection group. The lower the sNa, the more overcorrection was seen (2.4 times more overcorrection in the group with a baseline sNa of 110-115 meq/L and 6 times more overcorrection in the group with a sNa of <110 mEg/L). We found that low baseline sodium levels are associated with overcorrections of hyponatremia, which is in agreement with previous studies [17,20,21,24]. However, in these studies, baseline sNa levels of< 125 mEg/L were not divided into sub-groups. In one study, sNa<120 mmol/L was reported as an independent risk factor for overcorrection [15]. Tailoring the treatment approach according to baseline sNa levels may be effective in preventing overcorrection.

In addition to lower baseline sNa, in previous studies, younger age, higher infusion volume, and low baseline serum potassium levels have been identified as risk factors for overcorrection of hyponatremia [17,24,25]. In our study, a minimum of 3 administration of 3% NaCl 150 ml and high creatinine were risk factors for overcorrection.

Limitations

This study has some limitations. This is a single-center retrospective study conducted only in the emergency department. Data loss is high. No randomization was made and treatment decisions were left to the consideration of the treating physicians in the Emergency Department. The hypertonic saline treatment groups were not equally distributed. Overcorrection is reported to be one of the major causes of ODS; however, it can also be caused by chronic alcoholism and liver disease [9, 19]. Among the patients whose hyponatremia was overcorrected in our study, 20.5% did not have ODS. This might be attributed to both our exclusion criteria and the fact that we only followed up the patients in the emergency department. Since the hospitalized patients were not followed up, we do not have data on whether ODS developed on days 5-10.

Conclusion

In the treatment of symptomatic hyponatremia with 3% NaCl, a target serum Na of 125 mmol/L may be used in addition to a 5 mmol/L increase in serum Na. The volume status of the patient, baseline serum Na levels, and RIB treatment have been effective in achieving the target values. In the prevention of overly rapid serum Na elevation, 3% NaCl treatment in a smaller volume than baseline serum Na levels < 125 mmol/L may be considered.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

The authors declare no conflict of interest.

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This study was approved by the Ethics Committee of Ege University (Date: 2023-01-13, No: 23-1T/41)